Original Article

Evaluation of Preemptive Use of Analgesia of The Skin, Before and After Lower Abdominal Surgery: A Prospective, Double-Blind, Randomized Clinical Trial

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ABSTRACT

Background: Perioperative pain is prevalent and poorly treated. Apart from that it makes the recovery from surgery unpleasent, pain often remains as a residual side effect of surgery, even though the tissue healing is complete. An essential observation is that tissue injury and the resulting nociceptor barrage initiates a cascade of events that can indelibly alter pain perception. Preemptive analgesia is the concept of initiating analgesic therapy before the onset of the noxious stimulus so as to prevent the nociceptor barrage and its consequences. However, anticipated clinical potency of preemptive analgesia, though has firmly grounded in the neurobiology of pain, has not been yet realized. As data accumulates, it has become clear that clinical studies emulating those from the laboratory and designed around a relatively narrow definition of preemptive analgesia have been largely unsupportive of its use. Nevertheless, preemptive analgesic interventions that recognize the intensity, duration, and somatotopic extent of major surgery can help reduce perioperative pain and its longer-term sequelae. surgeons spend a lot of time treating the pain of lower abdominal surgery.

Methods: A total number of 48 consecutive patients who were going to undergo elective lower abdominal surgery. Were randomly assigned in two groups of 24 each. In one group the patients received an injection of 0.5 % bupivacaine in the planned skin for incision just before lower abdominal surgery, and in the other group, they received an equal amount of 0.5% bupivacaine after the surgery had been done. Pain was objectified by a numerical visual pain score, in the 24 hours following the lower abdominal surgery.

Results: There were no differences in postoperative pain scores on the visual analog scale (VAS): In groups 1and 2, VAS at hour 4 were 6.37±1.13 versus 6.29±1.19; At hour 8 were 5.54 ± 1.17 versus 5.37±1.09; and at hour 12 were 4.5 ± 1.31 versus 4.45 ± 1.1 respectively (P-value was not significant). There was not any difference between the main of morphine consumption between the two groups: at 12 hours, they were 11 ±3.5 versus 11.5 ±3.63; and at 24 hours, they were 17.87±5.88 versus 18.29 ±5.85 (P-value was not significant).

Conclusions: The administration of local anesthesia prior to starting surgery does not appear to have any advantage over its postoperative administration in patients undergoing lower abdominal surgery.

Keyword: analgesia, bupivacaine, preemptive, postoperative.

Adequate analgesia is important postoperatively and is particularly important in patients undergoing ambulatory surgery. It has previously been demonstrated that up to one third of patients suffer from moderate to severe postoperative pain due to inadequate analgesia. On-demand intramuscular opiates fail to produce adequate pain relief for more than 80% of Patients [1, 2, 3, 4, 5, 6]. Apprehension of potential adverse side effects and addiction has contributed to underutilization of prescribed opiates and attention has focused on other methods of achieving analgesia such as the use of local anesthetic agents and nonsteroidal anti-inflammatory drugs (NSAIDs). A combination of opioids, NSAIDs, and local anesthetic agents provides good pain relief. This combination is effective for pain relief in day-case surgery. However, the question remains is to determine the optimum schedule for administration of these agents. The concept of preemptive analgesia has gained popularity; and a previous study of this institute demonstrated the value of preemptive use of

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tenoxicam, an NSAID, that may be administered intravenously[7].

Experimental studies with animal pain models have demonstrated that brief noxious stimuli, which are perceived as pain, may result in long-lasting neuronal sensitization. When this sensitization occurs, innocuous stimuli may be perceived as pain. Surgical procedures, even skin incisions, may result in this initial sensitization. These observations on the genesis and perception of pain led to the concept that analgesia administered before an initial noxious stimulus may be more effective than the same dose given afterwards.

Concepts for control of postoperative pain have progressed as a result of the discovery that early control of pain can alter its subsequent evolution, the recognition that nociception produces important physiological responses even in adequately anesthetized individuals, and an understanding that for many patients, minimization of pain can improve clinical outcomes[8,9].

In spite of a sound theoretical base and encouraging animal studies, the clinical value of preemptive analgesia remains to be fully evaluated because there are very controversies in the results of previous study. This study was established to examine the value of preemptive bupivacaine in patients undergoing lower abdominal surgery under general anesthesia.

Subjects and Methods

In this prospective, randomized study, pain scores and analgesic requirements were examined in 48 patients who were going to undergo undergoing elective minor lower abdominal surgery (herniorrhaphy, varicocelectomy, hydrocele, …). All patients were ASA I or II, 15-65 years old, and have no history of addiction and premedication with analgesic drugs. Each patient was given an informed consent for participation in the study, which was approved by the local ethics committee.

The patients were enrolled and randomized according to the table of random numbers, which was opened prior to induction. The patients who were assigned to group A, received 0.4ml/kg of 0.5% bupivacaine (regarding previous study and safe dose) approximately 5 minutes before incision. The patients who were assigned to group B, received the same dose after skin closure, while still anesthetized. Patients with change in surgical and anesthetic plan and analgesic requirement were excluded from study.

All patients received a standard anesthesia and no premedication was administered. Patients were induced with fentanyl(2 g/kg),thiopental (5 mg/kg), and atracurium (0.5 mg/kg). Anesthesia was maintained with 50 percent nitrous oxide and oxygen, adding inhaled agent 0.8 halothane. The patients also received intravenous morphine (0.1mg/kg) before incision and the choice of administered drug was left to the discretion of the recovery nurse who had no knowledge of the group to which the patient belonged.

A Performa was completed for all the patients detailing name, medical records number, age, sex, pain scores at 4, 8, and 12 hours and morphine consumption (12-24 hours) postoperatively. The pain score was assessed using a visual analogue scale (VAS), and these were scored from 0 to 10 cm (0 cm, no pain; 10 cm, worst possible pain). An investigator, without any knowledge of the group to which the patient belonged, recorded pain scores and analgesic requirements.

A formal sample size calculation was performed. From previous work, the standard deviation of VAS pain scores was approximately 1.5 cm. A two-sided significance level of 0.05 and a power of 80% were used with a specified mean difference of 1 cm. The calculated sample size was 24 patients in each group. All enrolled patients completed the study. Statistical analysis was performed using the ANOVA and the Mann-Whitney U test. Significance was assumed at the 5% level.

Results

A total of 48 patients were enrolled in the study. There were 24 patients in group A (preincision bupivacaine) and 24 patients in group B (postoperative bupivacaine).

There was no significant difference between the two groups with respect to age and sex of the patients (58.33% male ,41.67% female, mean age of patients: 38.4±2.34 years). There were no differences in postoperative pain scores on the visual analog scale (VAS) between two groups: VAS at hour 4 were 6.37±1.13 versus 6.29±1.19, and P-value wasn't significant; VAS at hour 8 were 5.54 ± 1.17 versus 5.37±1.09, and P-value wasn't significant; VAS at hour 12 were 4.5±1.31 versus 4.45± 1.1, and P-value wasn't significant. There was no difference in the main of morphine consumption between the two groups:

at 12 hours, they were 11 ±3.5 versus 11.5±3.63; and at 24 hours, they were 17.87± 5.88 versus 18.29± 5.85, and P-value wasn't significant. No significant differences were observed between the two groups with respect to pain scores at 4, 8, and 12 hours, postoperatively (Table 1). In addition, no significant differences were observed in need for additional analgesia and dose of administered morphine (Table 1).

Table1. Postoperative pain scores (12 hours) and morphine consumption (24 hours) in the two groups

Variable	First Group (1)	Second Group (2)	
	Mean±SD	Mean±SD	P-Value
VAS at 4 h	6.37 ± 1.13	6.29 ± 1.19	0.106
VAS at 8 h	5.54 ± 1.17	5.37 ±1.09	0.614
VAS at 12h	4.50 ± 1.31	4.45 ± 1.10	0.906
Morphine (mg) used at 12 h	11.0 ± 3.50	11.50 ± 3.63	0.630
Morphine (mg) used at 24 h	17.87 ± 5.88	18.29 ± 5.85	0.807

Discussion

The present study demonstrated no benefits for preincisional infiltration with bupivacaine compared with the same dose of bupivacaine administered postoperatively. The timing of delivery of bupivacaine did not influence pain scores, additional analgesia requirements, or time to first analgesia.

Experimental animal studies have demonstrated that well-localized and brief noxious stimuli, perceived as pain, result in long-lasting neuronal sensitization resulting from alterations in central process of stimuli, with reduction in threshold, amplification of responses, expanded receptive fields, and after-discharges of dorsal horn neurons. Mechanical, chemical, or thermal threats to tissue integrity activate nociceptors and initiate a local inflammatory response[10, 11]. The noxious stimuli and the host response sensitize functional nociceptors and/or activate dormant ones. Sensitized nociceptors have an increased rate of basal discharge, a lowered stimulus threshold, and a supranormal increase in discharge rate with each increase in stimulus strength, or have a combination of these changes to produce sensitization. Endogenous analgesic responses are also mobilized along with processes of pain amplification, and the balance between these processes may determine the responses of an individual after injury.

When sensitization occurs-and it has been suggested that surgical trauma may lead to these alterations-innocuous stimuli may be perceived as pain. These observations lead to the concept that analgesia administered before an initial noxious stimulus (e.g. skin incision) that may produce neuronal sensitization is more effective than the same dose given afterwards, i.e., the concept of preemptive analgesia. In spite of a well-established theoretical base and promising experimental studies, the clinical value of preemptive analgesia remains to be fully realized.

Pasqualucci performed a review of preemptive studies, both experimental and clinical, that specifically examined local anesthetic agents[12]. Nineteen studies were identified, 8 experimental and 11 clinical. In only 3 of the 8 experimental studies, comparing preadministration versus postadministration of local anesthetic agents, real preemptive analgesia effect were demonstrated. Four of 11 clinical studies were positive and seemed to confirm the validity of the preemptive concept. Failure of many studies to demonstrate a preemptive effect when using local anesthetic agents was attributed to the inadequacy of the analgesic levels reached and maintained in the preoperative and intraoperative period. In the present study a standard dose of 0.4ml/kg of 0.5 % bupivacaine was employed. A larger dose may have proven more benefit but the same dose was employed in both arms of the study. It has also been

hypothesized that extending the preemptive treatment well into the postoperative period using balanced, multimodal analgesia, may prolong the initial advantage conferred by the preoperative blockade[13]. Initial perioperative control of pain may have long-term benefits. In adults, meticulous perioperative analgesia for radical prostatectomy lowered analgesic requirement and improved functional status for months postoperatively[14]. The biological and psychological foundation for persistent postoperative pain may be in place within hours of injury[15].

Many investigators examining the value of preemptive local anesthetics have examined oral surgery and found it to be of little benefit[16, 17]. Dierking et al examined a preoperative versus a postoperative inguinal field block using lidocaine in patients undergoing herniorrhaphy and found no significant differences between the groups for pain scores, time to first analgesia, or total morphine consumption[18]. Holthusen et al compared preoperative with postoperative caudal blocks in patients undergoing circumcision and found no benefit[19]. These two studies were small, with 32 patients in the first and 25 in the second, and may have lacked power.

Dahl et al randomized 50 children undergoing hernioplasty to preincisional or postoperative bupivacaine groups [20]. Apart from a lower anesthetic requirement and a reduced postoperative pain level after 30 minutes, there was no difference between infiltration before (preemptive) or after surgery, and there were no differences between the two groups regarding need for additional analgesia. A similar lack of effect was seen in the present study.

The ability to demonstrate a preemptive analgesic effect depends on the interaction of multiple factors. These include the extent and nature of the tissue damage, the duration of surgery, agents used preemptively, their route and timing of administration and their duration of action, the extent of afferent blockade, the ability of other agents given during surgery to preempt postoperative pain, and the time course of central sensitization, all of which interact with the emotional, physiological, and psychological state of the patient[21,22].Small differences in the initial state of the patient and in the intensity, quality, and meaning of the nociceptive stimulus can produce major differences in the final perceptions of pain[23,24]. Many of these factors are difficult to control in clinical studies and may account for some of the discrepancies between studies on preemptive analgesia[25, 26].

In conclusion, the administration of bupivacaine prior to starting surgery, as a preemptive analgesic agent, does not appear to have any clinical advantages over its postoperative administration in patients undergoing lower abdominal surgery.

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